



# Method of detection of pathological areas in biotissues on the basis of determination of characteristics of harmonic components in an ultrasonic wave

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The task of improving the quality of methods of ultrasound examination of the human body is relevant today. Analyze the existing methods of visualization of internal structures of biological objects was carried out in the paper. Investigated ultrasonic-based method of higher harmonics of the acoustic waves transmitted through the biological environment, which allows to increase the contrast, resolution and the accuracy of determining the location of the object. The proposed method is based on the analysis of the secondary acoustic field at the observation point M. The mathematical calculations have shown that the changes in the nonlinear parameter in the medium coincide with the distribution of the amplitudes of the oscillatory velocities of the wave of the secondary field. The developed method of ultrasonic visualization based on the determination of the amplitude parameters of the secondary field of the passed acoustic wave can be used to construct an image of a plane slice of a biological object.

## INTRODUCTION

Modern methods of treatment of cancer patients in the early stages of the disease, such as HIFU - therapy, allow non-invasive removal of metastases and small tumors in the pelvic organs and breast. The powerful focused ultrasound used for this purpose should be directed precisely to the pathological area, so as not to damage healthy tissues.<sup>1,2</sup> The existing methods of imaging the internal structures of a person in order to detect pathological changes in organs and tissues and to determine their size and place of origin due to physical reasons are ineffective in the early stages, or cannot be used during medical procedures. It is necessary to look for ways of visualization, allowing both real-time therapy and observe the results of therapeutic effects.<sup>3-5</sup>

## MATERIALS AND METHODS

The most common methods of non-invasive imaging of internal structures of biological objects are x-ray, computer and magnetic resonance imaging and ultrasonic research. X-ray computed tomography is a high-contrast method due to a significant difference in the absorption of ionizing radiation by different tissues. However, such radiation is ionizing to the body and in excess of the dose can cause the development of pathological tumors. Magnetic resonance imaging is a

highly accurate and safer method compared to x-ray, but has a number of limitations, such as: overweight patient, various types of heart failure, as well as the presence of built-in pacemakers and defibrillators. Based on the above, it can be concluded that ultrasound imaging of internal structures of the body are the most accessible and safe, as well as allow monitoring the development of pathologies.<sup>1,2,4</sup>

However modern methods of ultrasound based on echolocation principles have significant drawbacks concerning the quality of visualization, such as: low contrast and low resolution, as well as changing the direction of the beam when passing through the interface of media.<sup>5,6</sup> Ultrasonic-based studies of higher harmonics of the acoustic waves transmitted through the biological environment, enhance the contrast, resolution and the accuracy of determining the location of the object.<sup>6,7</sup>

The process of formation of higher harmonics of the passed acoustic wave is based on nonlinear properties of biological tissues.<sup>8,9</sup> When the ultrasonic wave passes through a nonlinear medium, the particles of the medium in the compression and vacuum zones move at different speeds, which leads to distortion of the profile of the vibrational velocity of the acoustic wave. As a result, harmonic components appear in the main signal.<sup>6</sup>

Description of the process of nonlinear interaction is mathematically possible by adding nonlinear terms to the right side of the wave equation used to describe the passage of an ultrasonic wave through a biological object, shown in figure 1.<sup>6,7,10</sup>

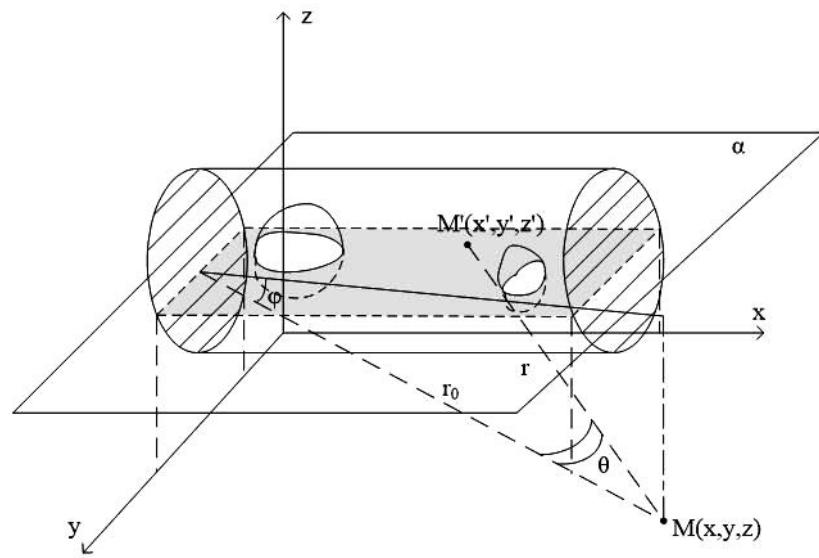
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$$\frac{\partial^2 \varphi}{\partial t^2} - c_0^2 \Delta \varphi = L_2(v^2) + L_3(v^3) + \dots$$

**Figure 1** Wave equation with nonlinear terms



1-muscle tissue,

2-pathological tissue (fibroids)

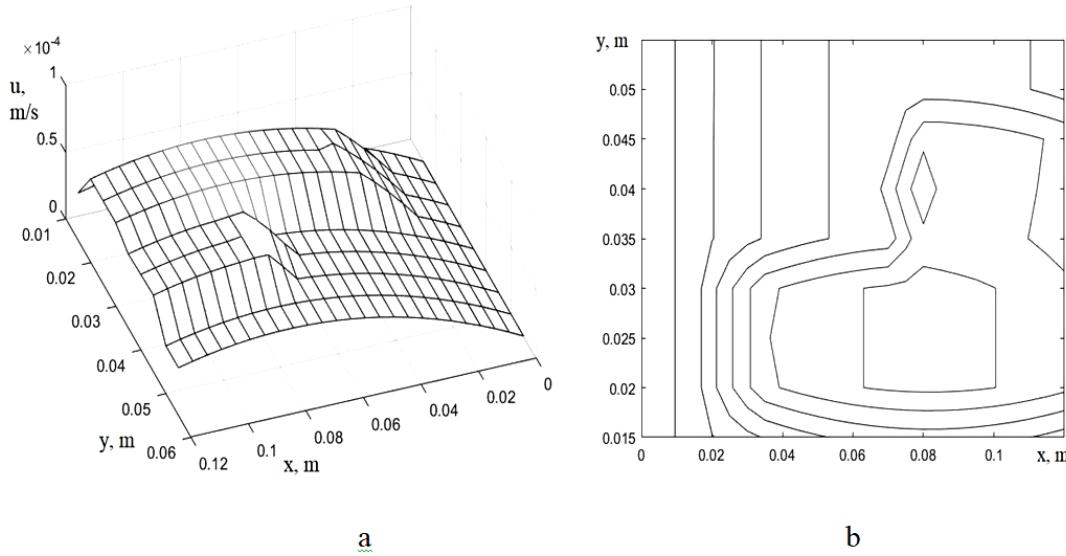
**Figure 2** Scheme of spatial arrangement of biotissue phantom with inhomogeneities

$$U(2\omega) = \frac{\omega u_0^2 r_0}{2c_0^2} \iiint_V \epsilon_i \cos(\alpha + \beta x' + \gamma y' + \eta z') dx dy dz = \\ = \frac{\omega u_0^2 r_0}{2c_0^2} \int_{b_1}^{b_2} \epsilon_z dz' \int_{l_1}^{l_2} \epsilon_x dx \int_{a_1}^{a_2} \epsilon_y (\cos(+\beta x' + \gamma y' + \eta z')) dz'.$$

**Figure 3** Equation describing the field of secondary sources of the second harmonic of the acoustic wave at the observation point M

$$\begin{aligned}
u(r) = & \frac{\varepsilon}{2c_0^2} \omega u_0^2 r \cos\left(2\omega\left(t - \frac{r_0}{c_0}\right)\right) \sin\left(\frac{l_2 - l_1}{2} k^{2\omega} (\cos\theta - 1)\right) \times \\
& \times \sin\left(\frac{b_2 - b_1}{2} k^{2\omega} \sin\varphi\right) \sin\left(\frac{a_2 - a_1}{2} k^{2\omega} \sin\theta\right) \cos\left(\frac{a_2 + a_1}{2} k^{2\omega} \sin\theta\right) \times \\
& \times \cos\left(\frac{l_2 + l_1}{2} k^{2\omega} (\cos\theta - 1)\right) \sin\left(\frac{b_2 + b_1}{2} k^{2\omega} \sin\varphi\right) \times \\
& \times \left[ \left(1 - \tan\left(\frac{a_2 + a_1}{2} k^{2\omega} \sin\theta\right)\right) - \left(1 + \tan\left(\frac{a_2 + a_1}{2} k^{2\omega} \sin\theta\right)\right) \right] - \\
& - \frac{\varepsilon}{2c_0^2} \omega u_0^2 r \sin\left(2\omega\left(t - \frac{r_0}{c_0}\right)\right) \frac{4}{k^{2\omega} (\cos\theta - 1) k^{2\omega} \sin\theta k^{2\omega} \sin\varphi} \times \\
& \times \frac{2}{k^{2\omega} \sin\varphi} \sin\left(\frac{l_2 - l_1}{2} k^{2\omega} (\cos\theta - 1)\right) \sin\left(\frac{l_2 + l_1}{2} k^{2\omega} (\cos\theta - 1)\right) \times \\
& \times \cos\left(\frac{a_2 + a_1}{2} k^{2\omega} \sin\theta\right) \sin\left(\frac{a_2 - a_1}{2} k^{2\omega} \sin\theta\right) \sin\left(\frac{b_2 - b_1}{2} k^{2\omega} \sin\varphi\right) \times \\
& \times \left[ \cos\left(\frac{b_2 + b_1}{2} k^{2\omega} \sin\varphi\right) - \sin\left(\frac{b_2 - b_1}{2} k^{2\omega} \sin\varphi\right) \times \right. \\
& \left. \times \cos\left(\frac{b_2 - b_1}{2} k^{2\omega} \sin\varphi\right) \right] \left[ \left(1 - \frac{\tan\left(\frac{a_2 + a_1}{2} k^{2\omega} \sin\theta\right)}{\tan\left(\frac{l_2 + l_1}{2} k^{2\omega} (\cos\theta - 1)\right)}\right) - \right. \\
& \left. - \left( \tan\left(\frac{a_2 + a_1}{2} k^{2\omega} \sin\theta\right) + \cot\left(\frac{l_2 + l_1}{2} k^{2\omega} (\cos\theta - 1)\right) \right) \right].
\end{aligned}$$

**Figure 4** The result of the integration



**Figure 5** Distribution of amplitudes of oscillatory velocities of the secondary sources field in a flat section of the object

The characteristic parameters of the propagation of higher harmonics of an acoustic wave passing through a biological object depend on the value of the nonlinear parameter of a particular medium.<sup>7-10</sup>

Figure 2 shows a model for obtaining information indicators of the acoustic field distribution in the selected section at the observation point M.

In general, the equation describing the field of secondary sources of the second harmonic of the acoustic wave at the observation point M is presented in figure 3.<sup>11-14</sup>

In this equation:  $r_0$  – distance from the origin located in the nonlinear interaction region to the observation point;  $c_0$  – phase sound velocity;  $u_0$  – initial value of the vibrational velocity of the first harmonic;  $\varepsilon = (\gamma+1)/2$ ,  $\gamma$  – the nonlinear parameter of the medium;  $\omega =$

$2\pi f$  – cyclic frequency of the basic harmonic;  $\tau = t - (r/c_0)$  – time in the accompanying coordinate system.

To obtain the amplitude distribution of the oscillatory velocities of the secondary field, the expression shown in figure 3 is integrated over three spatial coordinates. The result of integration is shown in figure 4.<sup>15-17</sup>

The resulting expression allows us to describe the field of secondary sources concentrated in the field of nonlinear interaction of an acoustic wave with biological tissue. On the basis of dynamics of change of the amplitudes of the vibration velocities at different value of the nonlinearity parameter of the tissue to determine the location and size of nascent pathological growths.<sup>17-20</sup>

Working with a three-dimensional model is a very difficult task, therefore, in the framework of mathematical modeling, the case is considered, reduced to a plane slice  $\alpha$ . On the basis of measuring the amplitude of the vibrational velocity in the cross section, using the proposed mathematical apparatus, it is possible to obtain the distribution of the nonlinear parameter in the cross section, which allows to determine the size and coordinates of the pathological region. The changes in the amplitude parameters of the field of secondary sources during the passage of an ultrasonic wave through a heterogeneous biological medium consisting of muscle tissue ( $\gamma = 2,6$ ) and pathological inclusions (fibroid,  $\gamma = 8,83$ ), according to the location shown in figure 2.

## RESULTS

The results of the calculations are presented in the form of a three-dimensional surface graph (figure 5 a) showing the change in the amplitude of the vibrational velocity of the secondary field of the passed acoustic wave and contour plot (figure 5 b) displaying the coordinates of the secondary radiation sources in space along the x and y axes. The graph clearly shows the presence of areas of pathological inclusions, the nonlinear parameter of which is higher in comparison with the surrounding tissues.

## DISCUSSION

The calculations have shown that the distribution of the amplitudes of the vibrational velocities of the secondary field coincides with the change of nonlinear parameters of the tissue in a flat section. The results obtained correspond to the basic laws of formation and propagation of higher harmonics of an acoustic signal passing through a nonlinear biological medium. Also, the calculations showed that the second harmonic of the acoustic wave passing through a biological object is sensitive even to small changes in the nonlinear parameter of tissues.

## CONCLUSION

The developed method of ultrasonic visualization based on the determination of the amplitude parameters of the secondary field of the passed acoustic wave can be used to construct an image of a plane slice of a biological object. The results obtained allow us to assert that ultrasonic methods based on the determination of parameters of nonlinear interaction of acoustic wave with biological tissues are a promising area of research in the field of medical ultrasound diagnostics.

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**Article Keywords**

Ultrasound imaging, nonlinear parameter, higher harmonics

**Authors Participation & Declaration**

Nikolay N. Chernov has investigated the method of ultrasonic imaging based on analysis of the characteristics of the secondary field of the passed acoustic wave. Mathematical model of the method which is the basis of simulation was developed. This method is based on the interaction of an acoustic wave with nonlinear biological tissues. The final text of the article has been edited by Nikolay N. Chernov.

Anastasia Yu. Varenikova has analyzed existing visualization techniques based on radiation of different nature. Has carried out a research of a ways to improve the quality of ultrasound imaging. Made a conclusion about the relevance of the use of methods of nonlinear acoustics in the field of ultrasonic research.

Margarita V. Laguta has carried out mathematical modeling of changes in the parameters of the secondary acoustic field, which are emerging in the result of the interaction of acoustic radiation with nonlinear biological tissue having inhomogeneities. Performed analysis of the distribution of the amplitude characteristics of the secondary acoustic field relative to the distribution of the nonlinear parameter in a biological object.

The results of mathematical calculations and modeling conducted in this study have not been previously published in other publications and are not under consideration for publication.

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